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Validation of Fourier Amplitude Ratio to Quantitate Valvular Regurgitation

P. TODD MAKLER, JR., MD, FACC, DAVID M. McCARTHY, MD, FACC,
JOSEPH P. KLEAVELAND, MD, JOHN U. DOHERTY, MD, MICHAEL G. VELCHIK, MD

Philadelphia, Pennsylvania

It has previously been shown that patients with valvular regurgitation can be identified by the ratio of left and right ventricular amplitude values obtained from first harmonic Fourier analysis of the gated blood pool scan. The present study was designed to validate the accuracy of this technique for quantifying the amount of valvular regurgitation. In a blinded analysis of 19 patients who underwent cardiac catheterization, there was a close correlation between the radionuclide and hemodynamic determination of the amount of regurgitation (r = 0.84). The interobserver agreement for calculating the radionuclide data was also high (r = 0.88). These results suggest that the Fourier ventricular amplitude ratio is an accurate and reproducible technique for quantifying valvular regurgitation by gated blood pool scanning.

The degree of valvular regurgitation can be quantified at the time of cardiac catheterization by comparing the total (angiographic) and forward (Fick) stroke volumes of the left ventricle and calculating the regurgitant fraction (1). Noninvasive radionuclide methods of quantifying valvular regurgitation have been described (2–8), but the anatomic overlap of the right atrium and right ventricle on the equilibrium gated blood pool scan makes delineation of chamber borders difficult, leading some groups to recommend the use of specialized collimators (7) or functional images (5,7).

Utilizing first harmonic Fourier analysis of the gated blood pool scan, we developed a new method for assessing valvular regurgitation. The method involves calculating the ratio of left and right ventricular amplitude values (from the amplitude image). Initial results have shown that this ventricular amplitude ratio provides clear separation between patients with and without regurgitation (9).

The purpose of the present study was to evaluate the accuracy of the ventricular amplitude ratio technique in quantifying the amount of valvular regurgitation. The results of the technique were compared with the data obtained during cardiac catheterization and with an alternative radionuclide determination of valvular regurgitation based on the stroke count ratio.

Methods

Patients. The study group comprised 19 consecutive patients who met the following inclusion criteria: left-sided valvular insufficiency, absence of right-sided valvular insufficiency and undergoing both cardiac catheterization and equilibrium blood pool scans within 10 days of each other (Table 1). Six additional patients met the inclusion criteria but were excluded from the analysis because of technical inadequacy of the catheterization data (four patients) or the gated blood pool scan (two patients). Technical problems with the catheterization data were insufficient opacification of the left ventricle (three patients) and erroneous oximetry data (one patient); the technical problem with the radionuclide data was the inability to identify the ventricular regions on the amplitude image (both patients).

Included in the analysis are 14 men and 5 women, with a mean age of 55 years (range 33 to 72). Ten patients had mitral regurgitation, six had aortic regurgitation and three had combined mitral and aortic regurgitation. The mean interval between cardiac catheterization and gated blood pool scanning was 3.8 days (range 1 to 10). Two patients were in atrial fibrillation at the time of their evaluation.

Cardiac catheterization. Catheterization was performed in the fasting state, using either a femoral or brachial artery approach, or both. To calculate the Fick cardiac output, central aortic and pulmonary artery blood samples were

From the Departments of Radiology (Nuclear Medicine) and Medicine (Cardiology), University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania. This study was supported in part by Training Grant HL07346 from the National Heart, Lung, and Blood Institute, Bethesda, Maryland. Manuscript received January 25, 1983; revised manuscript received December 9, 1983, accepted December 15, 1983.

Address for reprints: P. Todd Makler, Jr., MD, Department of Radiology, Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, Pennsylvania 19104.

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Table 1. Findings From Cardiac Catheterization and Radionuclide Blood Pool Scans in 19 Consecutive Patients With Left-Sided Valvular Insufficiency

		Catheterization			Radionuclide		
Case	Diagnosis	EDV (ml)	LVEF (%)	SVR	LVEF (%)	VAR	SCR
1	MR	283	65	3.70	62	3.33	3.27
2	MR, AR	333	20	1.64	22	1.92	1.09
3	MR	269	36	2.04	32	2.17	2.01
4	MR	317	24	2.00	22	1.92	1.34
5	MR	202	50	2.13	44	2.44	2.79
6	AR	170	45	1.37	50	1.79	1.51
7	MR, AR	283	65	2.50	72	2.22	6.46
8	MR	445	12	1.52	22	1.79	4.44
9	MR	195	78	1.64	86	1.20	1.00
10	AR	263	27	2.22	20	2.17	2.46
11	AR	213	65	1.89	70	1.59	1.26
12	MR	138	40	2.13	35	2.22	3.41
13	AR	149	46	1.16	50	1.35	1.95
14	MR, AR	255	.65	1.92	58	1.92	2.32
15	AR	244	62	1.64	63	1.59	1.84
16	MR	228	48	2.50	57	2.23	6.00
17	MR	188	40	1.37	46	1.17	2.34
18	MR	228	48	2.04	38	1.23	2.38
19	AR	163	39	1.56	40	1.61	2.49

AR = aortic regurgitation; EDV = end-diastolic volume; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; SCR = stroke count ratio; SVR = stroke volume ratio; VAR = ventricular amplitude ratio.

obtained and oxygen saturation and hemoglobin concentration measured to determine oxygen content. Forward cardiac output was determined from the measured arteriovenous oxygen difference across the lungs and an estimate of oxygen consumption based on the patient's age, sex, body surface area and heart rate (10). Forward (Fick) stroke volume was then calculated as forward cardiac output divided by heart rate at the time of blood sampling.

Left ventriculography was performed in the 20 to 30° right anterior oblique projection after the injection of 45 cc of Renografin-76 into the left ventricle. The cineangiogram was recorded on 35 mm film at 60 frames/s. The distances from image intensifier to the X-ray tube and to the patient were recorded to determine the magnification correction factor. Tracings of the end-diastolic and end-systolic ventricular contours were obtained by planimetry and the respective volumes were calculated by the single plane area-length method of Sandler and Dodge (11) and the Kennedy regression formula (12). In the two patients in atrial fibrillation, a beat of normal cycle length which followed a beat with an average RR interval was selected. Total stroke volume was defined as end-diastolic volume minus end-systolic volume.

The catheterization stroke volume ratio (SVR) is the ratio of the total stroke volume to the forward stroke volume. The catheterization (cath) regurgitant fraction (RF) is calculated as:

$$\text{Cath RF} = \frac{\text{Total stroke volume} - \text{Forward stroke volume}}{\text{Total stroke volume}}$$

$$= \frac{\text{Cath SVR} - 1}{\text{Cath SVR}}.$$

Equilibrium gated blood pool scanning. The patient's red blood cells were labeled in vivo with 20 mCi technetium-99m pertechnetate (13). The patient was positioned under a gamma camera equipped with a parallel hole collimator, and the 40° left anterior oblique view was modified if necessary to provide the "best septal" visualization. A multigated acquisition was obtained consisting of 24 frames (64 × 64 matrix) spanning the entire cardiac cycle, with 250,000 counts/frame and rejection of beats occurring after cycles outside a ± 10% RR interval window. The scan data were analyzed using a first harmonic Fourier analysis program distributed as part of the DEC Clinical Applications package. The method establishes two 64 × 64 functional images containing the phase and amplitude data (14,15). A time-activity curve is obtained from each pixel of the gated blood pool study, and the first Fourier harmonic of this time-activity curve provides an amplitude value and a phase shift value that are stored in the appropriate pixel locations in the functional images.

Figure 1 shows the blood pool and amplitude images obtained from Patient 1. In the amplitude image, the four cardiac chambers are clearly delineated as the four areas

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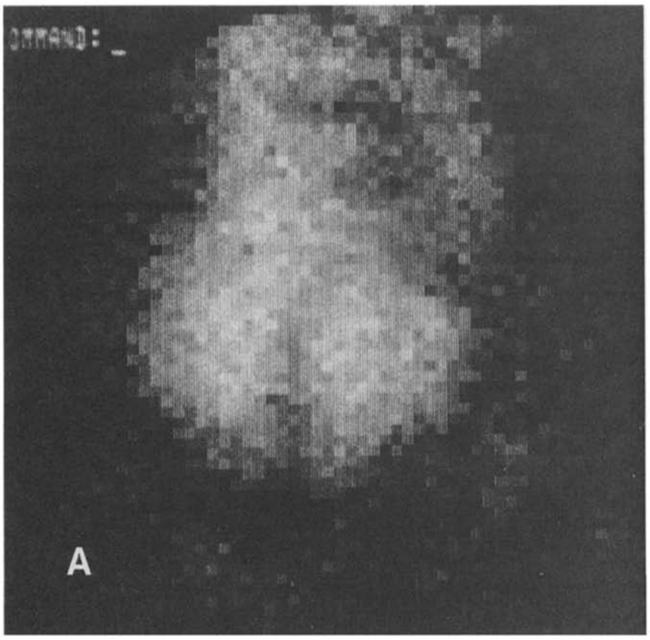
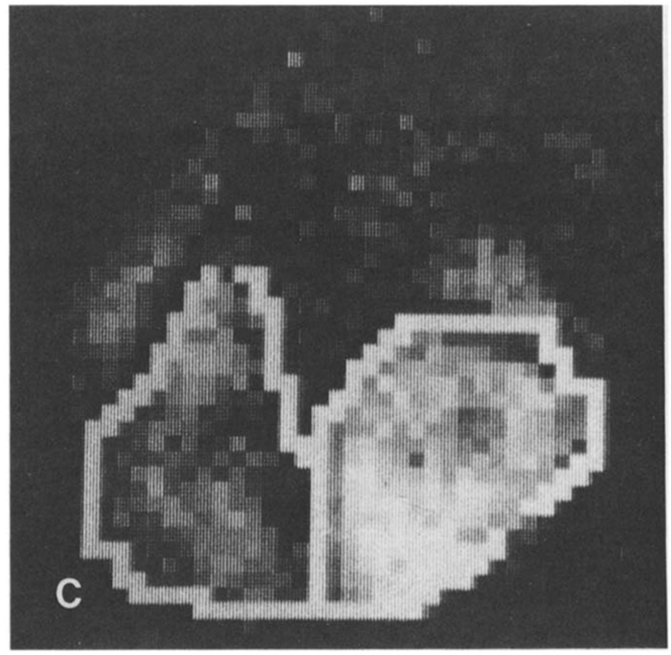




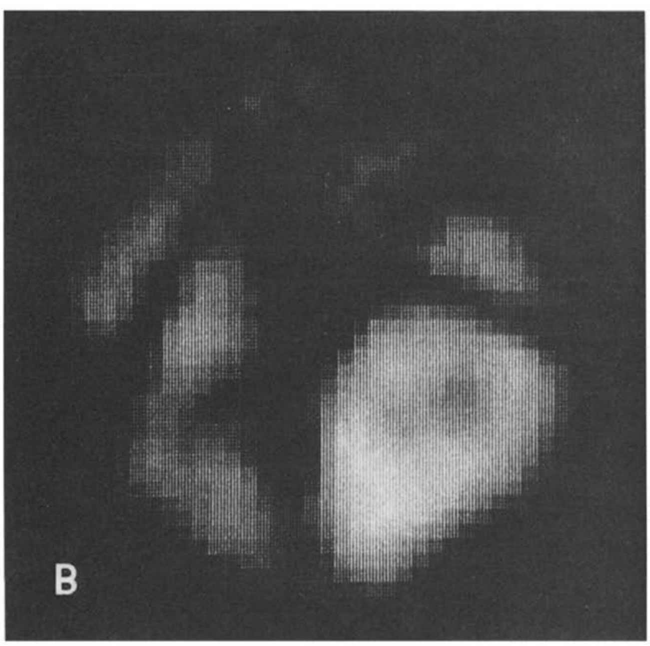


Figure 1. Case 1. **A**, End-diastolic blood pool image in the 40° left anterior oblique projection. **B**, Fourier amplitude image from the same subject. The four cardiac chamber images are clearly separable. **C**, Irregular regions of interest defining the right and left ventricles on the amplitude image (**B**).

that have significant amplitude. To generate a ventricular amplitude ratio, an irregular region of interest was drawn around each ventricle in the amplitude image (Fig. 1C). In cases with very low stroke counts (and low amplitude values), the regions of interest were drawn to approximate the configuration of the ventricle as noted on the blood pool image. The regions of interest provide a total amplitude value for each ventricle, and the ventricular amplitude ratio is the ratio of these values (left to right). It should be stressed that this ratio is determined by directly calculating the ratio of total amplitude values in their regions of interest; the amplitude regions of interest are *not* applied to the blood pool image. Results with the ventricular amplitude ratio method have previously been reported from our laboratory (9). In 14 patients without evidence for valvular insufficiency, the ratio averaged 1.14 ± 0.11 (± standard deviation).

The radionuclide regurgitant fraction (scan RF) is calculated as:

$$\text{Scan RF} = \frac{\text{Ventricular amplitude ratio} - 1}{\text{Ventricular amplitude ratio}}.$$

The ventricular amplitude ratio was calculated by one observer who was unaware of the catheterization data. Interobserver variation was assessed by having the data reanalyzed by a different observer.

To compare the ventricular amplitude ratio method with another radionuclide approach, the radionuclide stroke count ratio was determined by two observers. A fixed region of interest was established over each ventricle at end-diastole, and a time-activity curve was generated for each ventricle to determine the end-systolic frame. The stroke counts for each ventricle were the difference between the end-diastolic and end-systolic counts, and the stroke count ratio was the ratio of left to right stroke counts.

Statistical analysis. Data are expressed as the mean ± standard deviation. Differences between heart rate and ejection fraction at the time of cardiac catheterization and scanning were evaluated by Student's *t* test for paired observations. The results of catheterization and radionuclide scanning (stroke volume ratio, ventricular amplitude ratio, stroke count ratio and regurgitant fraction) were correlated using linear regression techniques, as was interobserver variation.

Results

The mean heart rate during cardiac catheterization (Fick = 84.9 beats/min; angiography = 82.0 beat/min) was not significantly different from that at the time of radionuclide scanning (83.5 beats/min). Similarly, the left ventricular ejection fraction by angiography (46.5 ± 18.2%) and scan (45.7 ± 20.9%) did not differ significantly.

Table 1 summarizes the catheterization and radionuclide results. Figure 2 compares the results of the catheterization stroke volume ratio and the radionuclide ventricular amplitude ratio. The two techniques correlated closely (r = 0.84, standard error of the estimate [SEE] = 0.29) with a slope (0.78) close to unity. Interobserver agreement was high for the ventricular amplitude ratio calculation (r = 0.88, SEE = 0.25, Fig. 3). The regurgitant fractions calculated by each of the techniques are shown in Figure 4. Again, there is a high degree of correlation (r = 0.69, SEE = 0.11).

The stroke count ratio from fixed region of interest analysis was also determined in these 19 patients. Although the interobserver agreement with this approach was good (r = 0.61, SEE = 1.61), the correlation with the catheterization stroke volume ratio was poor (r = 0.44, SEE = 1.27, Fig. 5). The standard error of the estimate for the stroke count ratio analysis was markedly greater than that obtained with the ventricular amplitude ratio technique.

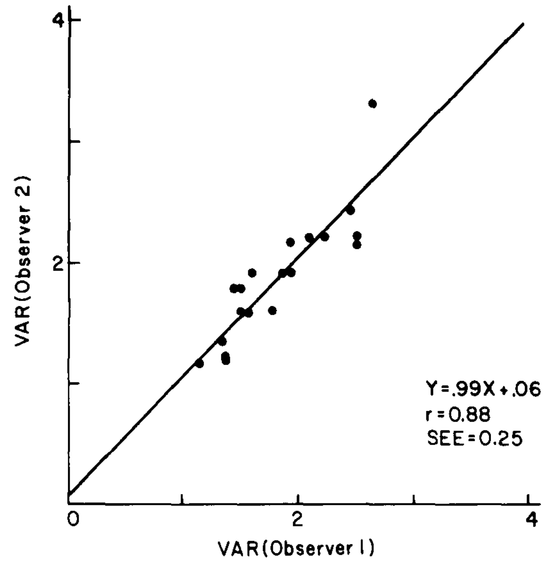


Figure 3. Results calculated by two independent observers, showing high interobserver agreement. VAR = Fourier ventricular amplitude ratio.

Discussion

Methodologic problems. There have been many attempts to quantify the severity of valvular insufficiency using a variety of nuclear medicine techniques (2–8,16,17). The problem intrinsic to direct analysis of the blood pool data lies in the definition of the right ventricular boundaries (18). Although the right ventricular boundary can usually be defined at end-diastole, boundary definition at end-systole is difficult because of overlap of the right ventricle and right atrium.

Figure 2. Correlation between cardiac catheterization (Cath) and radionuclide results. SVR = stroke volume ratio by catheterization; VAR = Fourier ventricular amplitude ratio.

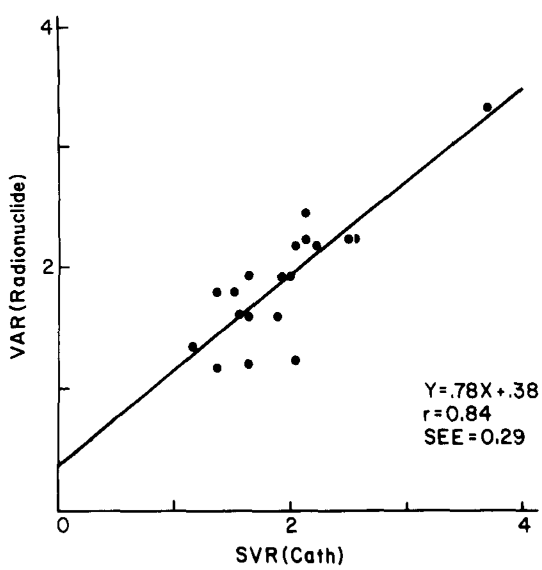
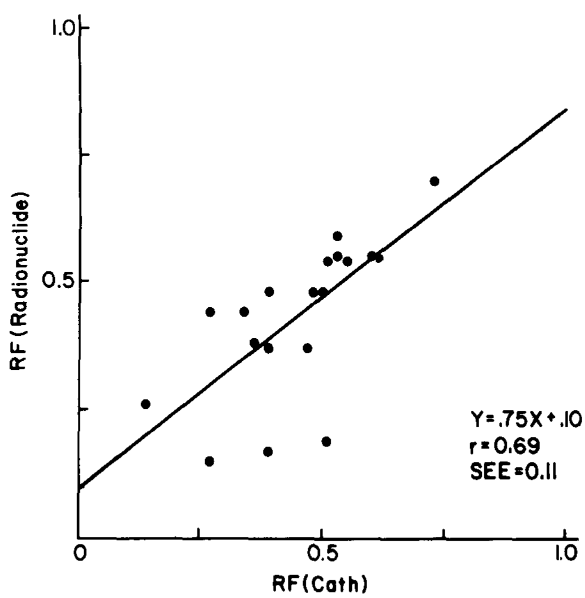


Figure 4. Correlation between cardiac catheterization (Cath) and radionuclide regurgitant fraction (RF).



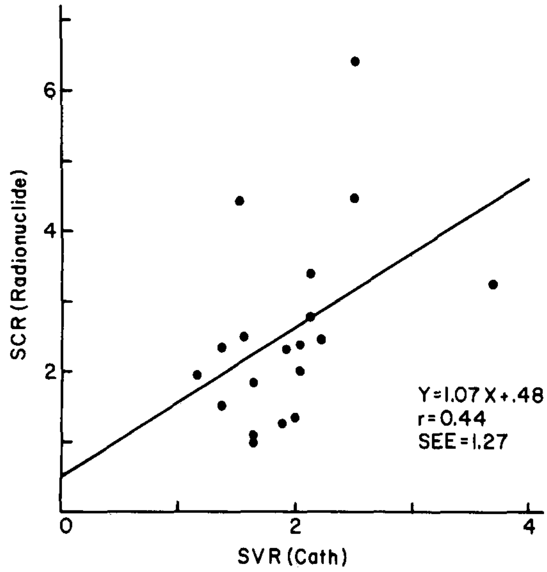


Figure 5. Correlation between catheterization stroke volume ratio (SVR [Cath]) and standard fixed region of interest stroke count ratio (SCR) from gated blood pool scanning.

Ventricular stroke counts can be determined using either a single (fixed) end-diastolic region of interest or separate (variable) end-diastolic and end-systolic regions of interest. Nicod et al. (17) compared these methods and found that the fixed region of interest approach had the best reproducibility (9.1% interobserver variability) and sensitivity (74% for 2^+ or greater valvular insufficiency), whereas the variable region of interest method was less reproducible (19.2% interobserver variability) and less sensitive (55%). The severity of insufficiency (as determined by the angiographic magnitude) did not, however, correlate with the calculated regurgitant index by either method. Our results analyzing the blood pool data with a fixed region of interest technique are similar (Fig. 5). Nicod et al. (17) did achieve marginally better results by direct analysis of a functional image (the stroke volume image), but even with this method they were unable to consistently differentiate between 2^+, 3^+ and 4^+ valvular regurgitation.

Another problem with direct analysis of the blood pool data is that the observed stroke count ratio (left to right) can be significantly elevated in normal subjects. Lam et al. (5) and Nicod et al. (17) studied normal subjects with ratios greater than 2.0. Recently, Henze et al. (8) reported a modification of the variable region of interest approach, in which normal subjects had a stroke count ratio of 1.01 ± 0.14 (± standard deviation). However, the interobserver variability was such that they cautioned against using their method to monitor changes in a given patient.

The ventricular amplitude technique to quantitate valvular regurgitation. We previously observed that the ventricular amplitude ratio can reliably separate normal subjects from those with severe valvular insufficiency and that the interobserver variability with this technique is low (9). This technique is based on the premise that first harmonic Fourier analysis of a gated blood pool study generates an amplitude value for each pixel which is a function of the stroke counts of that pixel. By summing all the amplitude values for each ventricle, one obtains a ventricular amplitude value that should be proportional to the ventricular stroke counts. In our series of 14 normal subjects, 16 patients with coronary artery disease and 17 patients with valvular insufficiency, the ventricular amplitude ratio was 1.14 ± 0.11, 1.22 ± 0.18 and 2.31 ± 0.77, respectively. There was no significant overlap between the 17 patients with valvular regurgitation and the other 30 patients. Among 14 normal subjects in our laboratory, the highest ventricular amplitude ratio value was 1.42 and the inter- and intraobserver variability were low. We thus believe that this ratio can reliably identify patients with valvular insufficiency.

The present study was designed to determine whether the ventricular amplitude ratio analysis could accurately quantify the magnitude of valvular insufficiency. The 19 patients constitute a consecutive series in whom reliable angiographic and Fick cardiac output determinations were obtained and in whom a gated blood pool study was performed in close temporal proximity. The results demonstrate a close correlation between the degree of valvular insufficiency at catheterization and ventricular amplitude ratio analysis.

Advantages of the ventricular amplitude ratio technique. This technique gives a reproducible and accurate estimate of the degree of valvular insufficiency. It is advantageous when compared with cardiac catheterization because the noninvasive nature of the method lends itself to serial evaluation of patients with a chronic and progressive cardiac condition.

The technique has high interobserver agreement (similar to fixed region of interest analysis of blood pool data) because the changes in ventricular volume are estimated by defining a single region of interest (on the amplitude image) for each ventricle. The technique has, however, the advantage of providing an accurate estimate of the magnitude of valvular insufficiency.

The anatomic overlap of the right atrium and right ventricle, of course, is not eliminated by the ventricular amplitude ratio technique; this accounts for our previous observation that the mean ratio in normal subjects was 1.14 ± 0.11. The cardiac chambers on the amplitude image, however, appear to be separate (Fig. 1), which facilitates region of interest selection and further enhances reproducibility.

Limitations of the study. The principal problem with our study is the use of the catheterization stroke volume as the reference standard. To calculate the catheterization stroke volume ratio requires accurate total stroke volume and forward cardiac output. Our catheterization laboratory routinely performs single plane angiography, which can be a source of error in the calculated total stroke volume, especially in patients with abnormally shaped ventricles (19). In addition, because our catheterization laboratory uses an assumed value for oxygen consumption (10), there is also a potential error in the calculated forward (Fick) stroke volume. Although actual measurement of oxygen consumption would be preferable, that datum was not available. Despite these potential drawbacks, however, the ventricular amplitude ratio technique correlated strongly with the catheterization results.

In addition to the 19 patients who constituted the study group, there were 2 patients who were excluded because their gated blood pool studies could not be adequately analyzed using the ventricular amplitude ratio approach. These two patients had a very low left ventricular ejection fraction (<20%) with a dilated left ventricle and severe wall motion abnormalities. In these cases, it was not possible to reliably determine the boundaries of the left ventricle on the amplitude image and, thus, an accurate ventricular amplitude ratio determination could not be obtained. Although in these two cases it was obvious that the data were unanalyzable, reliable data were obtained from other patients with poor left ventricular function (Table 1). Difficulty in evaluating blood pool data from patients with poor left ventricular function has been noted by Lam et al. (5) and Nicod et al. (17).

The first harmonic Fourier technique has been criticized as being a simplistic approach for analyzing radionuclide ventriculograms (20,21). Much of this criticism has been directed at the use of phase analysis to describe the sequence of ejection. Although the assumption that the first harmonic Fourier amplitude can describe pixel stroke counts is also simplistic, the present study suggests that it may be clinically useful.

Conclusion. A new approach to quantifying valvular regurgitation from radionuclide gated blood pool scans has been developed. The technique employs the amplitude image generated from first harmonic Fourier analysis. The method is reproducible and correlates with results obtained at cardiac catheterization. This technique may be useful in the serial evaluation of patients with valvular insufficiency.

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